

That which is claimed is:

1. Isolated nucleic acid encoding a Siah-Mediated-Degradation-Protein (SMDP) and/or SFC-Complex-Protein (SCP), or a functional fragment thereof.

5 2. Isolated nucleic acid encoding Siah-Mediated-Degradation-Protein (SMDP) and/or SFC-Complex-Protein (SCP), or functional fragments thereof, selected from:

(a) DNA encoding the amino acid sequence set forth in SEQ ID Nos:2, 4, 6, 8, 10, 12 or 14, or

10 (b) DNA that hybridizes to the DNA of (a) under moderately stringent conditions, wherein said DNA encodes biologically active SMDP and/or SCP, or

(c) DNA degenerate with respect to either (a) or (b) above, wherein said DNA encodes biologically active SMDP and/or SCP.

15 3. A nucleic acid according to claim 2, wherein said nucleic acid hybridizes under high stringency conditions to the SMDP and/or SCP coding portion of any of SEQ ID NOS:1, 3, 5, 7, 9, 11 and 13.

20 4. A nucleic acid according to claim 2, wherein the nucleotide sequence of said nucleic acid is substantially the same as set forth in any of SEQ ID NO:1, 3, 5, 7, 9, 11 and 13.

25 5. A nucleic acid according to claim 2, wherein the nucleotide sequence of said nucleic acid is the same as that set forth in any of SEQ ID NOS:1, 3, 5, 7, 9, 11 and 13.

6. A nucleic acid according to claim 2, wherein said nucleic acid is cDNA.

7. A vector containing the nucleic acid of
claim 2.

8. Recombinant cells containing the nucleic acid
of claim 2.

5 9. An oligonucleotide comprising at least 15
nucleotides capable of specifically hybridizing with a
the nucleotide sequence set forth in any of SEQ ID NOS:1,
3, 5, 7, 9, 11 and 13.

10 10. An oligonucleotide according to claim 9,
wherein said oligonucleotide is labeled with a detectable
marker.

11. An antisense-nucleic acid capable of
specifically binding to mRNA encoded by said nucleic acid
according to claim 2.

15 12. A kit for detecting the presence of the SMDP
and/or SCP cDNA sequence comprising at least one
oligonucleotide according to claim 10.

20 13. An isolated Siah-Mediated-Degradation-Protein
(SMDP) and/or SFC-Complex-Protein (SCP) characterized by
having ability to bind to at least one SMDP and/or SCP.

14. A SMDP and/or SCP according to claim 13,
wherein the amino acid sequence of said protein comprises
substantially the same sequence as any of SEQ ID Nos:2,
4, 6, 8, 10, 12 or 14.

25 15. A SMDP and/or SCP according to claim 14
comprising the same amino acid sequence as set forth in
any of SEQ ID Nos:2, 4, 6, 8, 10, 12 or 14.

16. A SMDP and/or SCP according to claim 13, wherein said protein is encoded by a nucleotide sequence comprising substantially the same nucleotide sequence as set forth in SEQ ID Nos:1, 3, 5, 7, 9, 11 or 13.

5 17. A SMDP and/or SCP according to claim 16, wherein said protein is encoded by a nucleotide sequence comprising the same sequence as set forth in SEQ ID Nos:1, 3, 5, 7, 9, 11 or 13.

10 18. A method for expression of a SMDP and/or SCP protein, said method comprising culturing cells of claim 8 under conditions suitable for expression of said SMDP and/or SCP.

15 19. An isolated anti-SMDP and/or SCP antibody having specific reactivity with a SMDP and/or SCP according to claim 13.

20. Antibody according to claim 19, wherein said antibody is a monoclonal antibody.

21. An antibody according to claim 20, wherein said antibody is a polyclonal antibody.

20 22. A composition comprising an amount of the antisense-nucleic acid according to claim 11 effective to inhibit expression of a human SMDP and/or SCP and an acceptable hydrophobic carrier capable of passing through a cell membrane.

25 23. A transgenic nonhuman mammal expressing exogenous nucleic acid encoding a SMDP and/or SCP.

24. A transgenic nonhuman mammal according to claim 23, wherein said nucleic acid encoding said SMDP and/or SCP has been mutated, and wherein the SMDP and/or SCP so expressed is not native SMDP and/or SCP.

5 25. A transgenic nonhuman mammal according to claim 23, wherein the transgenic nonhuman mammal is a mouse.

26. A method for identifying nucleic acids encoding a mammalian SMDP and/or SCP, said method comprising:

contacting a sample containing nucleic acids with an
10 oligonucleotide according to claim 9, wherein said
contacting is effected under high stringency
hybridization conditions, and identifying compounds which
hybridize thereto.

27. A method for detecting the presence of a human
15 SMDP and/or SCP in a sample, said method comprising
contacting a test sample with an antibody according to
claim 19, detecting the presence of an antibody-SMDP
and/or SCP complex, and therefor detecting the presence
of a human SMDP and/or SCP in said test sample.

20 28. Single strand DNA primers for amplification of
SMDP and/or SCP nucleic acid, wherein said primers
comprise a nucleic acid sequence derived from the nucleic
acid sequences set forth as SEQ ID NOS:1, 3, 5, 7, 9, 11
and 13.

25 29. A method for modulating the activity of an
oncogenic protein, comprising contacting said oncogenic
proteins with a substantially pure SMDP and/or SCP, or a
oncogenic protein-binding fragment thereof.

30. A bioassay for evaluating whether test compounds are capable of acting as agonists or antagonists for SMDP and/or SCP proteins, or functional fragments thereof, wherein said bioassay comprises:

- 5 (a) culturing cells containing:
 DNA which expresses an SMDP and/or SCP or functional fragments thereof,
 wherein said culturing is carried out in the presence of at least one compound whose ability
10 to modulate an activity of an SMDP and/or SCP is sought to be determined, wherein said activity is selected from a protein:protein binding activity or a protein degradation activity and thereafter
- 15 (b) monitoring said cells for either an increase or decrease in the level of protein:protein binding or protein degradation.

31. A method for modulating an activity mediated by a SMDP and/or SCP protein, said method comprising:

- 20 contacting said SMDP and/or SCP protein with an effective, modulating amount of said agonist or antagonist identified by claim 30.

32. The method of claim 31, wherein said modulated activity is the binding of Siah-1 to APC.

- 25 33. A method for modulating the protein degradation activity mediated by an SMDP and/or SCP protein, said method comprising:
 contacting said SMDP and/or SCP protein with an effective, modulating amount of said agonist or
30 antagonist identified by claim 30.

34. A therapeutic composition comprising a compound selected from an SMDP and/or SCP, or functional fragment thereof, a SMDP and/or SCP modulating compound identified according to claim 30, or an anti-SMDP and/or SCP antibody; and a pharmaceutically acceptable carrier.

35. A method of treating a pathology characterized by abnormal cell proliferation or abnormal inflammation, said method comprising administering an effective amount of the composition according to claim 34.

36. A method of inducing the degradation of the function of a target protein, said method comprising:
expressing, in a cell, a chimeric protein comprising a target-protein binding domain operatively linked to a protein-degradation binding domain of a protein member of the ubiquitin-mediated protein-degradation family.

37. The method of claim 36, wherein the protein-degradation binding domain is ornithine decarboxylase (ODC).

38. A method of determining the function of a target protein, said method comprising:
expressing, in a first cell, a chimeric protein comprising a target-protein binding domain operatively linked to a protein-degradation binding domain of a protein member of the ubiquitin-mediated protein-degradation family; and
comparing the phenotype of said first cell to the phenotype of a control second cell.

39. The method of claim 38, wherein the protein-degradation binding domain is ornithine decarboxylase (ODC).

40. A method of identifying a nucleic acid molecule
5 encoding a protein that modulates a cellular phenotype,
said method comprising:

- 10 (a) expressing, in a cell, a chimeric nucleic acid comprising a member of a nucleic acid library fused to nucleic acid encoding a protein degradation binding domain of a protein member of the ubiquitin-mediated protein degradation family; and
- (b) screening said cells for a modulation of said phenotype.

41. The method of claim 40, wherein the phenotype
15 is selected from the group consisting of: cell proliferation, cell survival, cell death, cell secretion, and cell migration.

42. A chimeric nucleic acid identified according to
claim 40.

20 43. A nucleic acid library comprising a plurality of chimeric nucleic acids, wherein each chimeric nucleic acid comprises an SMDP and/or SCP or functional fragment thereof.

25 44. The method of claim 40 wherein said nucleic acid encoding a protein degradation binding domain is selected from the group consisting of Sia-1 α , SIP-L, SIP-S, SAF-1, SAF-2, and SAD, or functional fragments thereof.

45. A method for treating a disease by degrading the function of a target protein comprising:

introducing, into a cell, a chimeric protein comprising a target-protein binding domain operatively linked to a protein-degradation binding domain of a protein member of the ubiquitin-mediated protein-degradation family.

46. A chimeric protein comprising the SMDP and/or SCP of claim 13.